PALM INTRANET

Day : Tuesday
Date: 7/6/2004
Time: 09:10:25

Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
Additionally, enter the **first few letters** of the Inventor's First name.

Last Name	First Name	
Orson	Frank	Search

To go back use Back button on your browser toolbar.

Back to PALM | ASSIGNMENT | OASIS | Home page

Refine Search

Search Results -

Term	Documents
(13 NOT 5).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	48
(L13 NOT L5).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	48

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: Huang-Leaf.in.

Refine Search

Recall Text | Clear | Interrupt

Search History

DATE: Tuesday, July 06, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L14	L13 not L5	48	L14
L13	L12 and ((DNA adj vaccine) or (genetic adj immunization))	50	L13
L12	L11 and (DNA or plasmid or vector)	889	L12
L11	(conjugation or conjugate) same ((antibody or Ab) and (polycationic or polyethylenimine or polyimmine or polylysine or PEI))	1021	L11
L10	(Ab-PEI-DNA)	0	L10
L9	L7 and L3	1	L9
L8	L7 and L2	6	L8
L7	(Expression adj library) adj immunization	68	L7
L6	L5 and ((DNA adj vaccine) or (genetic adj immunization))	4	L6
L5	L2 and L3	43	L5

L4	L2 same L3	2	L4
L3	(polycationic or polyethylenimine or polyimmine or polylysine) same (conjugate)	1352	L3
L2	(aggregated or macroaggregated) same (protein or albumin or antibody)	5088	L2
L1	Orson-Frank-M$.in.	1	L1

END OF SEARCH HISTORY

Welcome to DialogClassic Web(tm)

Dialog level 04.11.00D
Last logoff: 01jul04 16:26:33
Logon file001 06jul04 11:25:52

***** ANNOUNCEMENT *****

***

--File 654 - US published applications from March 15, 2001 to the present are now online. Please see HELP NEWS 654 for details.

***

--File 581 - The 2003 annual reload of Population Demographics is complete. Please see Help News581 for details.

***

--File 990 - NewsRoom now contains February 2004 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains records from January 2003. The oldest months's records roll out of File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new OneSearch category.

***

--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.

***

*** --SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.

***

--Important Notice to Freelance Authors--
See HELP FREELANCE for more information

***

NEW FILES RELEASED
***MetalBase (File 36)
***AeroBase (File 104)
***DIOGENES: Adverse Drug Events Database (File 181)
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland (File 682)

***

UPDATING RESUMED

***

RELOADED
***Toxfile (File 156)
***Medline (Files 154-155)
***Population Demographics -(File 581)
***CLAIMS Citation (Files 220-222)

REMOVED

***

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<

****

KWIC is set to 50.
HILIGHT set on as ' '
* * * *

File 1:ERIC 1966-2004/Jun 09
(c) format only 2004 The Dialog Corporation

Set	Items	Description

```
Cost is in DialUnits
?
B 155, 159, 5, 73
       06jul04 11:26:41 User259876 Session D646.1
            $0.62    0.178 DialUnits File1
     $0.62  Estimated cost File1
     $0.20  INTERNET
     $0.82  Estimated cost this search
     $0.82  Estimated total session cost   0.178 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1966-2004/Jun W2
        (c) format only 2004 The Dialog Corp.
 *File 155: Medline has been reloaded. Accession numbers
have changed. Please see HELP NEWS 154 for details.
  File 159:Cancerlit 1975-2002/Oct
        (c) format only 2002 Dialog Corporation
 *File 159: Cancerlit ceases updating with immediate effect.
Please see HELP NEWS.
  File   5:Biosis Previews(R) 1969-2004/Jun W4
        (c) 2004 BIOSIS
  File  73:EMBASE 1974-2004/Jun W4
        (c) 2004 Elsevier Science B.V.

      Set  Items  Description
      ---  -----  -----------
?
S (AGGREGATED OR MACROAGGREGATED) (S) (PROTEIN OR ANTIBODY OR LIGAND OR ALBUMIN)
          37412  AGGREGATED
           1642  MACROAGGREGATED
        4188970  PROTEIN
        1308420  ANTIBODY
         310868  LIGAND
         279985  ALBUMIN
      S1   15417  (AGGREGATED OR MACROAGGREGATED) (S) (PROTEIN OR ANTIBODY
                  OR LIGAND OR ALBUMIN)
?
S S1 (S) (DNA OR VECTOR OR GENE OR (GENETIC (W) IMMUNIZATION))
          15417  S1
        2574560  DNA
         284815  VECTOR
        2492137  GENE
        1577250  GENETIC
         202627  IMMUNIZATION
            952  GENETIC(W)IMMUNIZATION
      S2    1278  S1 (S) (DNA OR VECTOR OR GENE OR (GENETIC (W)
                  IMMUNIZATION))
?
S S2 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENIMINE OR POLYIMMINE OR PEI)
           1278  S2
           2730  POLYCATIONIC
          10182  POLYLYSINE
              1  POLYETHELENIMINE
              0  POLYIMMINE
           3958  PEI
      S3      7  S2 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENIMINE OR
                  POLYIMMINE OR PEI)
?
RD
...completed examining records
      S4      3  RD (unique items)
?
T S4/3,K/ALL

  4/3,K/1     (Item 1 from file: 155)
```

DIALOG(R)File 155:MEDLINE(R)

12190474 PMID: 12526712
Novel shielded transferrin-polyethylene glycol-polyethylenimine/DNA complexes for systemic tumor-targeted gene transfer.
Kursa Malgorzata; Walker Greg F; Roessler Vanessa; Ogris Manfred; Roedl Wolfgang; Kircheis Ralf; Wagner Ernst
Pharmaceutical Biology-Biotechnology, Department for Pharmacy, Ludwig-Maximilians-Universitaet, Butenandtstrasse 5-13, D-81377 Muenchen, Germany.
Bioconjugate chemistry (United States) Jan-Feb 2003, 14 (1) p222-31, ISSN 1043-1802 Journal Code: 9010319
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Tumor-targeting **DNA** complexes which can readily be generated by the mixing of stable components and freeze-thawed would be very advantageous for their subsequent application as medical products. Complexes were generated by the mixing of plasmid **DNA** , linear polyethylenimine (PEI22, 22 kDa) as the main **DNA** condensing agent, PEG- **PEI** (poly(ethylene glycol)-conjugated **PEI**) for surface shielding, and Tf-PEG- **PEI** (transferrin-PEG- **PEI**) to provide a **ligand** for receptor-mediated cell uptake. Within the shielding conjugates, PEG chains of varying size (5, 20, or 40 kDa) were conjugated with either linear PEI22 (22 kDa) or branched PEI25 (25 kDa). The three polymer components were mixed together at various ratios with **DNA** ; particle size, surface charge, in vitro transfection activity, and systemic **gene** delivery to tumors was investigated. In general, increasing the proportion of shielding conjugate in the complex reduced surface charge, particle size, and in vitro transfection efficiency in transferrin receptor-rich K562 cells. The particle size or surface charge of the complexes containing the PEG- **PEI** conjugate did not significantly change after freeze-thawing, while complexes without the shielding conjugate **aggregated** . Complexes containing PEG- **PEI** conjugate efficiently transfected K562 cells after freeze-thawing. Furthermore the systemic application of freeze-thawed complexes exhibited in vivo tumor targeted expression. For complexes containing the luciferase reporter **gene** the highest expression was found in tumor tissue of mice. An optimum formulation for in vivo application, PEI22/Tf-PEG- **PEI** /PEI22-PEG5, containing plasmid **DNA** encoding for the tumor necrosis factor (TNF-alpha), inhibited tumor growth in three different murine tumor models. These new **DNA** complexes offer simplicity and convenience, with tumor targeting activity in vivo after freeze-thawing.

4/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11586546 PMID: 11741272
DNA/polyethylenimine transfection particles: influence of ligands, polymer size, and PEGylation on internalization and gene expression.
Ogris M; Steinlein P; Carotta S; Brunner S; Wagner E
Institute of Biochemistry, University of Vienna, Vienna, Austria. manfred.ogris@cup.uni-muenchen.de
AAPS pharmSci electronic resource (United States) 2001, 3 (3) pE21, ISSN 1522-1059 Journal Code: 100897065
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Receptor-binding ligands have been incorporated into **DNA**

/polyethylenimine (**PEI**) complexes to enhance cell binding and cellular internalization. This study characterizes receptor-mediated uptake of **DNA** / **PEI** complexes on a cellular basis. A novel assay based on flow cytometry was applied, discriminating between total cell-associated and extracellularly bound **DNA** complexes. Receptor-mediated uptake of **ligand** -containing **DNA** / **PEI** (molecular weight, 800 kd) complexes was found to occur quickly (within 1 hour), whereas unspecific uptake through adsorptive endocytosis is less efficient or requires extended periods to reach the same degree of internalization. Rapid, receptor-mediated internalization requires a small complex size; however, large, **aggregated** complexes show higher **gene** expression. Using **PEI** 25 kd conjugated to large proteins such as transferrin or antibodies, improper condensation with **DNA** leads to suboptimal uptake and **gene** expression, whereas partial replacement of **ligand** - **PEI** with unconjugated □PEI□ increases both uptake and transfection. In contrast, the 8 kd **protein** epidermal growth factor conjugated to **PEI** 25 kd properly condenses **DNA** and mediates specific uptake into human adenocarcinoma (KB) cells. Modification of the complex surface with appropriate amounts of poly(ethylene glycol) (PEG) does not block **ligand** -mediated internalization. A higher degree of PEGylation reduces the internalization of transferrin or **antibody** -containing complexes to a level similar to that of **ligand** -free complexes. In contrast, epidermal growth factor "mediated uptake is less effected by excessive PEGylation.

4/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11347280 PMID: 11437332
A small, synthetic peptide for gene delivery via the serpin-enzyme complex receptor.
Patel S; Zhang X; Collins L; Fabre J W
Department of Clinical Sciences, Guy's, King's and St Thomas' School of Medicine, King's College Hospital, London, UK.
journal of gene medicine (England) May-Jun 2001, 3 (3) p271-9, ISSN 1099-498X Journal Code: 9815764
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

BACKGROUND: The serpin-enzyme complex receptor (SECR) has previously been successfully targeted for **gene** delivery using synthetic peptide ligands covalently linked in fluid phase to commercially available **polylysine** preparations (approximately 10-54kDa). The objective of the present study was to improve this approach by the use of small, bifunctional, and easily standardised synthetic peptides. METHODS: Two synthetic peptides designated **polylysine** antitrypsin 1 (PAT1) (K16 FNKPFVFLI) and PAT2 (K16 CSIPPEVKFNKPFVFLI) were evaluated for **gene** delivery to the HUH7 human hepatocyte cell line. The K16 moiety binds **DNA** electrostatically, while the FVFLM motif of human alpha1-antitrypsin targets the SECR. RESULTS: Both PAT1 and PAT2 bind to and condense **DNA** into small particles as shown by laser scattering techniques. However, only PAT2 is effective for **gene** delivery, presumably on account of the greater distance between the K16 chain and the FVFLM motif. **Gene** delivery by PAT2/ **DNA** complexes is chloroquine-dependent, can be blocked completely by free **ligand** (CSIPPEVKFNKPFVFLI), and is highly efficient (e.g. approximately five-fold more effective than lipofectamine). At physiological salt concentrations, PAT2/ **DNA** complexes formed at 4 microg/ml **DNA** are approximately 350 nm in diameter and highly effective for **gene** transfer, but at 100 microg/ml **DNA** the complexes are **aggregated** (diameter > 4 microm) and inactive. CONCLUSIONS: A small (33 amino acid), bifunctional, synthetic peptide represents a highly efficient and readily standardised **DNA** **vector** for

the SECR. The effectiveness of this peptide depends on the distance of the K16 moiety from the targeting **ligand** . High salt concentrations are not required to form effective **vector** **DNA** complexes.
?

```
Set     Items   Description
S1      15417   (AGGREGATED OR MACROAGGREGATED) (S) (PROTEIN OR ANTIBODY OR
              LIGAND OR ALBUMIN)
S2       1278   S1 (S) (DNA OR VECTOR OR GENE OR (GENETIC (W) IMMUNIZATION-
             ))
S3          7   S2 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENIMINE OR -
              POLYIMMINE OR PEI)
S4          3   RD (unique items)
?
S S2 AND (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR POLYIMMINE OR PEI)
            1278  S2
            2730  POLYCATIONIC
           10182  POLYLYSINE
               3  POLYETHELENEIMINE
               0  POLYIMMINE
            3958  PEI
      S5       11  S2 AND (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE
                   OR POLYIMMINE OR PEI)
?
RD S5
...completed examining records
      S6        5  RD S5 (unique items)
?
S S6 NOT S3
               5  S6
               7  S3
      S7       2  S6 NOT S3
?
T S7/3,K/ALL
```

7/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12372498 PMID: 12749911
The phosphocholine and the polycation-binding sites on rabbit C-reactive protein are structurally and functionally distinct.
Black Steven; Agrawal Alok; Samols David
Department of Biochemistry, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106, USA.
Molecular immunology (England) Jun 2003, 39 (16) p1045-54, ISSN 0161-5890 Journal Code: 7905289
Contract/Grant No.: AG02467; AG; NIA; AR40765; AR; NIAMS; DK07319; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

C-reactive **protein** (CRP) is an acute phase **protein** in humans and rabbits that has the ability to bind a number of biologically important ligands including phosphocholine (PCh), histones, and polycations. In addition to this recognition function, **ligand** -complexed or **aggregated** CRP is capable of activating the classical complement pathway. We have generated two strains of transgenic mice in order to study CRP-binding to PCh and consequent complement activation. Based on crystallographic and mutagenesis studies in human CRP (huCRP), we mutated Phe66 and Glu81 in the rabbit CRP (rbCRP) **gene** and generated a strain of transgenic mice (F66Y/E81K), which expressed this variant form of rbCRP. We also mutated Tyr175 in rbCRP to generate transgenic...

... rbCRP are distinct but possibly overlapping. The conformational changes in the C1q-binding site of CRP to activate complement depend on the nature of the **ligand** and on the location of the **ligand** -binding site.
Descriptors: C-Reactive Protein--chemistry--CH; *C-Reactive Protein --metabolism--ME; *Complement Pathway, Classical; *Phosphorylcholine --metabolism--ME; **Polylysine** --metabolism--ME
Chemical Name: Cations; Histones; Polyamines; Polysaccharides, Bacterial; Serum Albumin, Bovine; polycations; polysaccharide C-substance (Streptococcus); Phosphorylcholine; **Polylysine** ; Lysine; Complement 1q; C-Reactive Protein

7/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10029483 PMID: 8146151
Utilization of modified surfactant-associated protein B for delivery of DNA to airway cells in culture.
Baatz J E; Bruno M D; Ciraolo P J; Glasser S W; Stripp B R; Smyth K L; Korfhagen T R
Department of Pediatrics, Medical University of South Carolina, Charleston 29425-3313.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Mar 29 1994, 91 (7) p2547-51, ISSN 0027-8424
Journal Code: 7505876
Contract/Grant No.: 45961; PHS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... lines the airway epithelium and creates a potential barrier to successful transfection of the epithelium in vivo. Based on the functional properties of pulmonary surfactant **protein** B (SP-B) and the fact that this **protein** is neither toxic nor immunogenic in the airway, we hypothesized that SP-B could be modified to deliver **DNA** to airway cells. We have modified native bovine SP-B by the covalent linkage of poly(lysine) (average molecular mass of 3.3 or 10...

... was determined by transfection of pulmonary adenocarcinoma cells (H441) in culture with the test plasmid pCPA-RSV followed by measurement of activity of the reporter **gene** encoding chloramphenicol acetyltransferase (CAT). Transfections were performed with **DNA** . **protein** complexes using poly(lysine)10kDa-SP-B ([Lys]10kDa-SP-B) or poly(lysine)3.3kDa-SP-B ([Lys]3.3kDa-SP-B), and results were compared with transfections using unmodified poly(lysine). **DNA** , unmodified SP-B. **DNA** , or□DNA□only. For [Lys]10kDa-SP-B.pCPA-RSV preparations, CAT activity was readily detectable above the background of [Lys]3.3kDa-SP-B or unmodified SP-B. The SP-B-poly(lysine) conjugates were effective over a broad range of **protein** -to- **DNA** molar ratios, although they were optimal at approximately 500:1-1000:1. Transfection efficiency varied with the tested cell line but was not specific to...

... spectrometry (FTIR). Results of FTIR indicated that the conformation of [Lys]10kDa-SP-B was comprised primarily of alpha-helical structure compared with a predominantly **aggregated** structure of unmodified poly(lysine). We conclude that poly(lysine) conjugates of SP-B effectively deliver **DNA** in vitro and may have utility as **DNA** delivery vehicles to the airway in vivo.
Descriptors: DNA, Recombinant--pharmacology--PD; *Drug Carriers --pharmacology--PD; * **Polylysine** --pharmacology--PD; *Proteolipids --pharmacology--PD; *Pulmonary Surfactants--pharmacology--PD; *Transfection --methods--MT

```
  Chemical Name: DNA, Recombinant; Drug Carriers; Phosphatidylethanolamines
;      Proteolipids;      Pulmonary      Surfactants;      Polylysine     ;
1,2-dielaidoylphosphatidylethanolamine; Chloramphenicol O-Acetyltransferase
?

Set     Items   Description
S1      15417   (AGGREGATED OR MACROAGGREGATED) (S) (PROTEIN OR ANTIBODY OR
             LIGAND OR ALBUMIN)
S2       1278   S1 (S) (DNA OR VECTOR OR GENE OR (GENETIC (W) IMMUNIZATION-
            ))
S3          7   S2 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENIMINE OR -
             POLYIMMINE OR PEI)
S4          3   RD (unique items)
S5         11   S2 AND (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR
             POLYIMMINE OR PEI)
S6          5   RD S5 (unique items)
S7          2   S6 NOT S3
?
S S1 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR POLYIMINES OR PEI)
           15417  S1
            2730  POLYCATIONIC
           10182  POLYLYSINE
               3  POLYETHELENEIMINE
               2  POLYIMINES
            3958  PEI
      S8      36  S1 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE
                  OR POLYIMINES OR PEI)
?
RD S8
...completed examining records
      S9      18  RD S8 (unique items)
?
S S9 AND (DNA OR VECTOR OR GENE)
              18  S9

         2574560  DNA
          284815  VECTOR
         2492137  GENE
     S10       3  S9 AND (DNA OR VECTOR OR GENE)
?
T S10/3,K/ALL

  10/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

12190474   PMID: 12526712
  Novel shielded transferrin-polyethylene glycol-polyethylenimine/ DNA
  complexes for systemic tumor-targeted gene transfer.
  Kursa Malgorzata; Walker Greg F; Roessler Vanessa; Ogris Manfred; Roedl
Wolfgang; Kircheis Ralf; Wagner Ernst
  Pharmaceutical Biology-Biotechnology, Department for Pharmacy,
Ludwig-Maximilians-Universitaet, Butenandtstrasse 5-13, D-81377 Muenchen,
Germany.
  Bioconjugate chemistry (United States) Jan-Feb 2003, 14 (1) p222-31,
ISSN 1043-1802 Journal Code: 9010319
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed

  Novel shielded transferrin-polyethylene glycol-polyethylenimine/ DNA
  complexes for systemic tumor-targeted gene transfer.
  Tumor-targeting DNA complexes which can readily be generated by the
mixing of stable components and freeze-thawed would be very advantageous
```

for their subsequent application as medical products. Complexes were generated by the mixing of plasmid **DNA** , linear polyethylenimine (PEI22, 22 kDa) as the main **DNA** condensing agent, PEG- **PEI** (poly(ethylene glycol)-conjugated **PEI**) for surface shielding, and Tf-PEG- **PEI** (transferrin-PEG- **PEI**) to provide a **ligand** for receptor-mediated cell uptake. Within the shielding conjugates, PEG chains of varying size (5, 20, or 40 kDa) were conjugated with either linear PEI22 (22 kDa) or branched PEI25 (25 kDa). The three polymer components were mixed together at various ratios with **DNA** ; particle size, surface charge, in vitro transfection activity, and systemic **gene** delivery to tumors was investigated. In general, increasing the proportion of shielding conjugate in the complex reduced surface charge, particle size, and in vitro transfection efficiency in transferrin receptor-rich K562 cells. The particle size or surface charge of the complexes containing the PEG- **PEI** conjugate did not significantly change after freeze-thawing, while complexes without the shielding conjugate **aggregated** . Complexes containing PEG- **PEI** conjugate efficiently transfected K562 cells after freeze-thawing. Furthermore the systemic application of freeze-thawed complexes exhibited in vivo tumor targeted expression. For complexes containing the luciferase reporter **gene** the highest expression was found in tumor tissue of mice. An optimum formulation for in vivo application, PEI22/Tf-PEG- **PEI** /PEI22-PEG5, containing plasmid **DNA** encoding for the tumor necrosis factor (TNF-alpha), inhibited tumor growth in three different murine tumor models. These new **DNA** complexes offer simplicity and convenience, with tumor targeting activity in vivo after freeze-thawing.

Descriptors: **DNA** --administration and dosage--AD; *Drug Carriers --chemistry--CH; * **Gene** Therapy; *Neoplasms, Experimental--therapy--TH; Animals; **DNA** --therapeutic use--TU; K562 Cells; Mice; Mice, Inbred Strains ; Molecular Weight; Polyethylene Glycols--chemistry--CH; Polyethyleneimine --chemistry--CH; Transfection; Transferrin--chemistry--CH; Treatment Outcome; Tumor...

Chemical Name: Drug Carriers; Polyethylene Glycols; Tumor Necrosis Factor ; Transferrin; Polyethyleneimine; **DNA**

10/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11586546 PMID: 11741272

DNA **/polyethylenimine transfection particles: influence of ligands, polymer size, and PEGylation on internalization and** gene **expression.**

Ogris M; Steinlein P; Carotta S; Brunner S; Wagner E
Institute of Biochemistry, University of Vienna, Vienna, Austria. manfred.ogris@cup.uni-muenchen.de

AAPS pharmSci electronic resource (United States) 2001, 3 (3) pE21, ISSN 1522-1059 Journal Code: 100897065
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

DNA **/polyethylenimine transfection particles: influence of ligands, polymer size, and PEGylation on internalization and** gene **expression.**

Receptor-binding ligands have been incorporated into **DNA** /polyethylenimine (**PEI**) complexes to enhance cell binding and cellular internalization. This study characterizes receptor-mediated uptake of **DNA** / **PEI** complexes on a cellular basis. A novel assay based on flow cytometry was applied, discriminating between total cell-associated and extracellularly bound **DNA** complexes. Receptor-mediated uptake of **ligand** -containing **DNA** / **PEI** (molecular weight, 800 kd) complexes was found to occur quickly (within 1 hour), whereas unspecific uptake through adsorptive endocytosis is less efficient or requires extended periods to reach the same degree of internalization. Rapid, receptor-mediated internalization

requires a small complex size; however, large, **aggregated** complexes show higher **gene** expression. Using **PEI** 25 kd conjugated to large proteins such as transferrin or antibodies, improper condensation with **DNA** leads to suboptimal uptake and **gene** expression, whereas partial replacement of **ligand** - **PEI** with unconjugated □PEI□ increases both uptake and transfection. In contrast, the 8 kd **protein** epidermal growth factor conjugated to **PEI** 25 kd properly condenses **DNA** and mediates specific uptake into human adenocarcinoma (KB) cells. Modification of the complex surface with appropriate amounts of poly(ethylene glycol) (PEG) does not block **ligand** -mediated internalization. A higher degree of PEGylation reduces the internalization of transferrin or **antibody** -containing complexes to a level similar to that of **ligand** -free complexes. In contrast, epidermal growth factor "mediated uptake is less effected by excessive PEGylation.

Descriptors: **DNA** --chemistry--CH; * **Gene** Transfer Techniques; *Polyethylene Glycols--chemistry--CH; *Polyethyleneimine; **DNA** --metabolism --ME; Drug Carriers; Endocytosis; Epidermal Growth Factor--chemistry--CH; Flow Cytometry; Genes, Reporter; Jurkat Cells; KB Cells; Ligands; Luciferase--genetics--GE; Luciferase--metabolism--ME...

Chemical Name: Drug Carriers; Ligands; Muromonab-CD3; Plasmids; Polyethylene Glycols; Transferrin; Epidermal Growth Factor; Polyethyleneimine; **DNA** ; Luciferase

10/3,K/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11347280 PMID: 11437332

A small, synthetic peptide for gene **delivery via the serpin-enzyme complex receptor.**

Patel S; Zhang X; Collins L; Fabre J W

Department of Clinical Sciences, Guy's, King's and St Thomas' School of Medicine, King's College Hospital, London, UK.

journal of gene medicine (England) May-Jun 2001, 3 (3) p271-9, ISSN 1099-498X Journal Code: 9815764

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A small, synthetic peptide for gene **delivery via the serpin-enzyme complex receptor.**

BACKGROUND: The serpin-enzyme complex receptor (SECR) has previously been successfully targeted for **gene** delivery using synthetic peptide ligands covalently linked in fluid phase to commercially available **polylysine** preparations (approximately 10-54kDa). The objective of the present study was to improve this approach by the use of small, bifunctional, and easily standardised synthetic peptides. METHODS: Two synthetic peptides designated **polylysine** antitrypsin 1 (PAT1) (K16 FNKPFVFLI) and PAT2 (K16 CSIPPEVKFNKPFVFLI) were evaluated for **gene** delivery to the HUH7 human hepatocyte cell line. The K16 moiety binds **DNA** electrostatically, while the FVFLM motif of human alpha1-antitrypsin targets the SECR. RESULTS: Both PAT1 and PAT2 bind to and condense **DNA** into small particles as shown by laser scattering techniques. However, only PAT2 is effective for **gene** delivery, presumably on account of the greater distance between the K16 chain and the FVFLM motif. **Gene** delivery by PAT2/ **DNA** complexes is chloroquine-dependent, can be blocked completely by free **ligand** (CSIPPEVKFNKPFVFLI), and is highly efficient (e.g. approximately five-fold more effective than lipofectamine). At physiological salt concentrations, PAT2/ **DNA** complexes formed at 4 microg/ml **DNA** are approximately 350 nm in diameter and highly effective for **gene** transfer, but at 100 microg/ml **DNA** the complexes are **aggregated** (diameter > 4 microm) and inactive. CONCLUSIONS: A small (33 amino acid), bifunctional, synthetic peptide

represents a highly efficient and readily standardised **DNA vector** for the SECR. The effectiveness of this peptide depends on the distance of the K16 moiety from the targeting **ligand** . High salt concentrations are not required to form effective **vector DNA** complexes.
Descriptors: **Gene** Transfer Techniques; *Receptors, Cell Surface --metabolism--ME
?

```
Set     Items   Description
S1      15417   (AGGREGATED OR MACROAGGREGATED) (S) (PROTEIN OR ANTIBODY OR
              LIGAND OR ALBUMIN)
S2       1278   S1 (S) (DNA OR VECTOR OR GENE OR (GENETIC (W) IMMUNIZATION-
             ))
S3          7   S2 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENIMINE OR -
              POLYIMMINE OR PEI)
S4          3   RD (unique items)
S5         11   S2 AND (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR
              POLYIMMINE OR PEI)
S6          5   RD S5 (unique items)
S7          2   S6 NOT S3
S8         36   S1 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR
              POLYIMINES OR PEI)
S9         18   RD S8 (unique items)
S10         3   S9 AND (DNA OR VECTOR OR GENE)
?
S (AB-PEI-DNA) OR (AB-PEI-VECTOR)
               0  AB-PEI-DNA
               0  AB-PEI-VECTOR
     S11       0  (AB-PEI-DNA) OR (AB-PEI-VECTOR)
?
S (EXPRESSION (W) LIBRARY (W) IMMUNIZATION)
         2265064  EXPRESSION
          143284  LIBRARY
          202627  IMMUNIZATION
     S12      71  (EXPRESSION (W) LIBRARY (W) IMMUNIZATION)
?
S S12 AND S1
              71  S12
           15417  S1
     S13       0  S12 AND S1
?
S S12 AND REVIEW
              71  S12
         1737797  REVIEW
     S14       5  S12 AND REVIEW
?
RD
...completed examining records
     S15       4  RD (unique items)
?
T S15/3,K/ALL

  15/3,K/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2004 BIOSIS. All rts. reserv.

0014924972   BIOSIS NO.: 200400295729
 Expression   library   immunization to discover and improve vaccine
 antigens
AUTHOR: Barry Michael A (Reprint); Howell Dasein P G; Andersson Helen A;
  Chen Jiang Li; Singh Rana A K
AUTHOR ADDRESS: Ctr Cell and Gene Therapy, Baylor Coll Med, 1 Baylor
  Plaza,BCM505, Houston, TX, 77030, USA**USA
AUTHOR E-MAIL ADDRESS: mab@bcm.tmc.edu
JOURNAL: Immunological Reviews  199 (1): p68-83 June 2004 2004
```

MEDIUM: print
ISSN: 0105-2896
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Citation
LANGUAGE: English

Expression library immunization **to discover and improve vaccine antigens**
DESCRIPTORS:
METHODS & EQUIPMENT: **expression library immunization** --
MISCELLANEOUS TERMS: ...Literature **Review**

15/3,K/2 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12221990 EMBASE No: 2003331777
Advances in the identification and characterization of protective antigens for recombinant vaccines against tick infestations
De la Fuente J.; Kocan K.M.
J. De la Fuente, Dept. of Veterinary Pathobiology, College of Veterinary Medicine, Oklahoma State University, Stillwater, OK 74078 United States
AUTHOR EMAIL: jose delafuente@yahoo.com
Expert Review of Vaccines (EXPERT REV. VACCINES) (United Kingdom) 2003, 2/4 (583-593)
CODEN: ERVXA ISSN: 1476-0584
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 77

...identified and characterized, discovery of new antigens remains the limiting step for improving the efficacy of tick vaccines. Recent technologies developed for gene discovery, including **expression library immunization** and evaluation of expressed sequence tags, show promise for rapid, systematic and global antigen screening and should provide a comprehensive approach to selection of candidate...
MEDICAL DESCRIPTORS:
drug synthesis; ectoparasite; mosquito; pathogenesis; infection control; drug determination; drug efficacy; treatment outcome; immunization; disease transmission; drug formulation; vaccination; human; clinical trial; **review** ; priority journal

15/3,K/3 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

12040256 EMBASE No: 2003151720
Enhanced efficacy of DNA vaccines against an intracellular bacterial pathogen by genetic adjuvants
Leclercq S.; Harms J.S.; Oliveira S.C.
S.C. Oliveira, Department of Biochem./Immunology, Federal University of Minas Gerais, Inst. for Investigation Immunology, Av Antonio Carlos 6627, Belo Horizonte-MG 30161-970 Brazil
AUTHOR EMAIL: scozeus@icb.ufmg.br
Current Pharmaceutical Biotechnology (CURR. PHARM. BIOTECHNOL.) (Netherlands) 2003, 4/2 (99-107)
CODEN: CPBUB ISSN: 1389-2010
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 97

...immunogens. Secondly, we reported the use of cytokine genes and genetic adjuvants that could improve the immunogenicity of target genes.

And finally, we discussed the " **Expression Library Immunization** "-(ELI) strategy and the recent results obtained against Brucella abortus infection.
MEDICAL DESCRIPTORS:
...bacterial virulence; DNA hybridization; cytokine production; cytotoxic T lymphocyte; muscle necrosis; muscle regeneration; immunostimulation; antigen presenting cell; drug potentiation; gene construct; CpG island; nonhuman; mouse; **review**

15/3,K/4 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

07436928 EMBASE No: 1998327856
DNA vaccines
Lai W.C.; Bennett M.
Dr. W.C. Lai, Department of Pathology, Texas Univ. Southwestern Med. Ctr., 5323 Harry Hines Blvd., Dallas, TX 75235-9072 United States
Critical Reviews in Immunology (CRIT. REV. IMMUNOL.) (United States) 1998, 18/5 (449-484)
CODEN: CCRID ISSN: 1040-8401
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 235

...induction of injury to muscles prior to injection of DNA to enhance gene expression. Vaccination performed using DNA without knowing beforehand the protective epitopes, using ' **expression library immunization** ', is discussed. While this field is bound to expand rapidly for future clinical applications, we try to point out potential pitfalls as well as advantages
...
MEDICAL DESCRIPTORS:
protein expression; helper cell; aerosol; gene expression; dna library; antigen presenting cell; dendritic cell; immune response; drug effect; cloning vector; nonhuman; mouse; rat; animal cell; **review** ; priority journal
?

Set	Items	Description
S1	15417	(AGGREGATED OR MACROAGGREGATED) (S) (PROTEIN OR ANTIBODY OR LIGAND OR ALBUMIN)
S2	1278	S1 (S) (DNA OR VECTOR OR GENE OR (GENETIC (W) IMMUNIZATION-))
S3	7	S2 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENIMINE OR -POLYIMMINE OR PEI)
S4	3	RD (unique items)
S5	11	S2 AND (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR POLYIMMINE OR PEI)
S6	5	RD S5 (unique items)
S7	2	S6 NOT S3
S8	36	S1 (S) (POLYCATIONIC OR POLYLYSINE OR POLYETHELENEIMINE OR POLYIMINES OR PEI)
S9	18	RD S8 (unique items)
S10	3	S9 AND (DNA OR VECTOR OR GENE)
S11	0	(AB-PEI-DNA) OR (AB-PEI-VECTOR)
S12	71	(EXPRESSION (W) LIBRARY (W) IMMUNIZATION)
S13	0	S12 AND S1
S14	5	S12 AND REVIEW
S15	4	RD (unique items)

?
COST
06jul04 11:42:52 User259876 Session D646.2
$3.11 0.971 DialUnits File155

```
                $1.68  8 Type(s) in Format  3
              $1.68  8 Types
       $4.79  Estimated cost File155
              $0.75    0.256 DialUnits File159
       $0.75  Estimated cost File159
              $5.25    0.937 DialUnits File5
                $1.75  1 Type(s) in Format  3
              $1.75  1 Types
       $7.00  Estimated cost File5
              $7.82    0.798 DialUnits File73
                $8.10  3 Type(s) in Format  3
              $8.10  3 Types
      $15.92  Estimated cost File73
              OneSearch, 4 files,  2.962 DialUnits FileOS
       $4.25  INTERNET
      $32.71  Estimated cost this search
      $33.53  Estimated total session cost   3.140 DialUnits
?
```

Return to logon page!